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ILLNESSES ASSOCIATED WITH EXPOSURE TO METHAMIDOPHOS IN CALIFORNIA 1982 - 1990

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Executive Summary

Cases associated with exposure to methamidophos reported to the California Pesticide Illness Surveillance Program (PISP) from 1982 through 1990 were reviewed as a response to concerns that this compound accounted for excessive number of illnesses in proportion to the amount of methamidophos used. A formal evaluation of the comparative risk of exposure to methamidophos and other organophosphate (OP) compounds was conducted by means of an epidemiologic comparison known as a case-control study. Cholinesterase (ChE) related illness cases were defined on the basis of symptoms compatible with depression of blood ChE accompanied by either laboratory evidence of depressed ChE levels or the presence of one or more symptoms specific enough to indicate the probable presence of ChE depression. The control or comparison group were selected from the remaining reported exposures on the basis of non-depressed blood ChE levels or the absence of compatible symptoms.

Background

The organophosphorus compound methamidophos was first synthesized in 1964 as an insecticide and acaricide with both contact and systemic effects. In 1990, California growers reported 7,431 applications of methamidophos involving 411,476 pounds of the material. The principal uses included vegetable row crops - 4,204 applications (57.4% of the total) and 110,888.6 pounds of methamidophos (26.9% of total); melons - 304 applications (4.1% of the total) and 96,915.3 pounds (23.6% of the total); cotton - 1,163 applications (15.8% of the total) and 104,816.5 pounds (25.5% of the total), and root vegetables - 1,072 applications (14.6% of the total) and 58,595.2 pounds (14.2% of the total).

Methamidophos demonstrates high toxicity in experimental studies in rodents and this has been confirmed by experience with its agricultural use. Although the effects of poisoning are usually reversible, recovery from cases of near fatal poisoning resulting from deliberate or accidental ingestion of methamidophos has sometimes been complicated by delayed onset of peripheral nerve damage (organophosphate induced delayed neuropathy [OPIDN]). This delayed clinical effect has not been reported following cases of accidental poisoning in the workplace. Some research studies have shown that slowing of nerve conduction is measurable in workers previously poisoned with methamidophos who had no symptoms of OPIDN.

Methods

Case review involved manual scrutiny of PISP files for all cases identified from the computer source files. Information extracted included symptoms present, exposure history, and cholinesterase data, where present. Methamidophos associated cases involving suspected systemic illness were then compared with a large data base on suspected systemic illnesses associated with other cholinesterase inhibiting compounds in California during the same 1982-1990 time period. As part of a separate project these cases were manually reviewed in an identical manner. Comparisons were made based on the relative frequency of illnesses related to ChE depression for exposures reported to methamidophos and for exposures reported to other OPs. The relative difference in frequency of ChE- related illness between the cases and controls was measured by calculating epidemiologic statistic known as the Odds Ratio (OR). The odds ratio can be roughly described as the odds that case subjects had exposure to methamidophos when compared to a group of controls defined by the absence of ChE-related illness.

Results

From 1982 through 1990, the PISP source file contained records for 321 suspected exposures to methamidophos, with 315 records containing sufficient information to classify the relationship between exposure and illness. Of the 315 exposures with sufficient information to classify, 88 (27.9%) involved methamidophos as the sole cholinesterase inhibitor present and 227 (72.1%) involved multiple

cholinesterase inhibitors. From the information available in the investigation files, all of the ChE-related illnesses were of the acute reversible type and no instance of delayed neuropathy was reported. Two hundred twenty-two (70.5%) met the criteria for inclusion in the case-control study file, including 37 subjects with ChE-related illness and 185 control subjects.

Methamidophos associated cases showed a significantly decreased frequency of ChE-related illness compared to other OPs in the overall case-control study file (OR=0.32, $p<10^{-5}$). This decrease was associated principally with the 201 exposures to mixtures of ChE-inhibitors containing methamidophos (OR=0.31, $p<10^{-5}$). The 21 subjects with exposure to only methamidophos did not differ significantly in frequency of ChE illness from subjects exposed to other single OP compounds (OR=0.60, p=0.394).

Application exposure - The 32 subjects with application exposure to methamidophos had a greater likelihood of ChE-related illness than the 283 subjects in other methamidophos exposure categories (OR=19.22, $p<10^{-5}$). In the case-control analysis, the 24 subjects with methamidophos application exposure had a greater likelihood of ChE-related illness than subjects with application exposure to other OP compounds (OR=3.14, p=0.035). This finding remained significant upon multivariate analysis of the case-control study file.

Drift exposure - The drift exposures had a marked tendency to involve cluster episodes. Nine such cluster episodes accounted for 203 (91.4%) of the 222 drift exposure cases to methamidophos. Five episodes, each involving fewer than 10 individuals, accounted for 16 cases and the remaining four episodes involving from 11 to 131 individuals accounted for 187 cases. The drift exposures associated with methamidophos had a significantly reduced risk of ChE-related illness compared to other methamidophos exposure categories (OR=0.18, p<10-5). However, the methamidophos exposures showed only a non-significant reduction in risk compared to drift exposure to other OPs in the case-control study file (OR=0.51, p=0.057).

Field residue exposure - The 55 field residue exposures had a non-significantly reduced risk of definite and probable illness compared to other methamidophos exposures (OR=0.36, p=0.136). Compared to other OPs in the case-control study file, field reentry exposures involving methamidophos cases showed a similar non-significant reduction in the risk of ChE-related illness (OR=0.23, p=1.65x10-4 by Yates' P^2). The only fatal case associated with exposure to methamidophos occurred in a field worker who entered a recently treated San Diego county tomato field (see case 1837-85, Table 7). He felt faint in the field and collapsed. Other workers who were not reported to be ill, transported him to a hospital in Mexico. An autopsy done at that hospital did not include evaluation of ChE levels and the exact relationship between his death and the methamidophos exposure could therefore not be determined.

Conclusion

The overall risk of ChE-related illness associated with exposure to methamidophos showed a reduction from that associated with other organophosphates reported to the California PISP system. This reduction in overall risk was attributable to the large percentage of methamidophos cases with relatively low risk drift exposures. For application associated methamidophos exposure, the risk of ChE-related illness appeared significantly increased compared to other OP compounds in the case-control study file.

Introduction

We reviewed cases associated with methamidophos reported to the California Pesticide Illness Surveillance Program (PISP) from 1982 through 1990 as a response to concerns that this compound accounted for excessive number of illnesses in proportion to the amount of methamidophos used.[a] A formal evaluation of the comparative risk of exposure to methamidophos and other organophosphate (OP) compounds is presented, abstracted from a case-control study evaluating the entire OP data base in the PISP.[1] Although abstracted from a case-control analysis, the data presented here focus principally on a single compound (methamidophos) rather than on the multiple exposure factors commonly evaluated in a case-control analysis.[2 3]

Chemical properties and uses

The organophosphorus compound methamidophos (trade names - Monitor® and Tamaron®; chemical name - *O*,*S*-dimethyl phosphoramidothioate) is a crystalline, colorless solid with a melting point of 54EC. Its vapor pressure is $3x10^{-4}$ mm Hg at 30EC, and it is highly soluble in aliphatic hydrocarbons, alcohols, ketones, and water. It was first synthesized in 1964 as an insecticide and acaricide with both contact and systemic effects. In 1990, California growers reported 7,431 applications of methamidophos involving 411,476 pounds of the material. The principal uses included vegetable row crops - 4,204 applications (57.4% of the total) and 110,888.6 pounds of methamidophos (26.9% of total); melons - 304 applications (4.1% of the total) and 96,915.3 pounds (23.6% of the total); cotton -1,163 applications (15.8% of the total) and 104,816.5 pounds (25.5% of the total), and root vegetables - 1,072 applications (14.6% of the total) and 58,595.2 pounds (14.2% of the total).[4]

Toxicologic properties

Animal tests indicate that methamidophos is highly toxic to mammals. Its acute oral LD50 is 31 mg/kg for male rats, 32 mg/kg for female rats, and 21 mg/kg for male weanling rats. Acute dermal LD50 values are 94 mg/kg and 85 mg/kg for adult male and female rats, respectively. Following cases of near fatal human poisoning methamidophos has been reported as a cause of *organophosphate induced delayed neuropathy* (OPIDN).[5] Results from animal and *in vitro* tests show that this effect is produced most readily by the D+ stereo isomer of methamidophos. Racemic formulations tested produced OPIDN only at doses greatly exceeding the LD50.[6 7]

Methods

We reviewed cases identifying methamidophos as one of the possibly related exposures. The methodology was similar to that used in previous reviews of other cholinesterase inhibitors.[8 9 10] Cases were extracted from the PISP source file for each year from 1982 through 1990 based upon identification of methamidophos in one of the pesticide identification fields. Cases originally classified as unrelated to pesticide exposure were also reviewed in order to identify individuals who were part of illness clusters involving suspected exposure to methamidophos. The extraction procedure did not differentiate cases identifying methamidophos as the primary pesticide from those identifying it as a secondary exposure. Case review involved manual scrutiny of PISP files, including pesticide episode investigation reports (PEIR), doctor's first report (DFR), pesticide illness reports (PIR) and priority investigation reports for all cases identified from the computer source files were reviewed manually in order to extract information on signs and symptoms of illness, exposure history, and cholinesterase data, where present. The review focused on systemic illness, but included reports of skin or eye injury, and exposed, asymptomatic individuals who sought medical evaluation to maintain complete listings of groups exposed in cluster illness episodes.

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[a] unpublished analysis, U.S. E.P.A., Office of Pesticide Programs

Coding of Demographic Information

In addition to information specifically related to work exposure and illness, we coded demographic variables not originally coded in the original PISP file. These included sex, age, and ethnicity (based on Hispanic vs. non-Hispanic surname). Standard industrial classification (SIC) codes[11 12 13] were used to identify categories of employment [major industrial divisions, and major subdivisions of agriculture].

Statistical methods and Selection of Case and Comparison Subjects

The case group was selected from the entire OP case file based on the occurrence of definite and probable illness and employment in an agricultural SIC code. For descriptive purposes, this group was termed the ChE illness group. The comparison, or control, group included all subjects from the OP case file employed in agriculture and classified as unlikely illness, or unrelated illness, asymptomatic without evidence of ChE depression. Also included in the comparison group were symptoms compatible to ChE effect with reported ChE activity within the normal population range as reported by the testing lab. For descriptive purposes, this group was termed the non-ChE effect group.

The SPSS/PC statistical analysis program[14] was used for analyzing the coded information by exposure and illness category. Possible biases in reporting by demographic categories were evaluated by comparing summary demographic information with previously published information about the California agricultural workforce.[15 16 17 18 19 20 21] The distribution of SIC categories represented by the study subjects was also evaluated to determine the percent of the total agricultural population represented compared to the SIC categories not represented among the study subjects. Reported annual average employment for each agricultural SIC code was derived from data gathered from state unemployment insurance tax records and data for each year between 1982 and 1990 published by the U.S. Bureau of Labor Statistics.[22]

The odds (odds ratio [OR])[23] of developing definite or probable illness following OP exposure was calculated for potential risk factors including pesticide application work, field work, drift exposure, and individual OP compounds that accounted for 10 or more reported exposures. A Yates' chi-square was used to evaluate statistical significance, except in cases, as specifically noted, for which one or more expected cell frequencies was less than or equal to five, a two tailed Fisher's exact test (FET) was used. In addition to the crude analysis described above, stepwise logistic regression analysis [24] was used to evaluate the effect of exposure risk factors, effect modifiers, and potential confounders identified in the crude analysis.

Results

From 1982 through 1990, the PISP source file contained records for 4,121 reports associated with suspected cases of systemic illness following exposure to one or more OP compounds, including 4,042 records containing sufficient information to classify the relationship between exposure and illness according to the above stated criteria. The 4,042 records containing sufficient information to classify the relationship between exposure and illness included 315 associated with exposure to methamidophos (Table 1).

Of the methamidophos group, 88 (27.9%) involved methamidophos as the sole cholinesterase inhibitor present and 227 (72.1%) involved multiple cholinesterase inhibitors. By crop, 219 (69.5%) involved applications to vegetable crops including broccoli, cauliflower, tomatoes, celery and peppers; 59 cases (18.7%) resulted from applications to cotton; and 20 (6.3%) involved applications on unspecified crops by workers employed by professional agricultural pest control firms. Seven (2.2%) cases resulted from applications to miscellaneous crops including grain, potatoes, and sugar beets. The remaining 10 cases involved exposure to methamidophos drift from applications on unspecified crops, including 5 occupational and 5 non-occupational exposures (see Table 6 and Table 7 below). Table 1 displays a breakdown of cases by illness and exposure category for the 315 methamidophos cases with sufficient information to judge the

relationship between exposure and illness. There were 32 application associated cases - including 7 resulting from direct exposure to methamidophos, 23 from routine applications, and two from documented violations of proper application procedure. There were 55 cases resulting from exposure to field residue and 223 resulting from possible exposure to methamidophos drift. The five remaining cases included 4 miscellaneous exposures (one case of accidental ingestion, two cases involving repair work on application related machinery, a case resulting from burning used container bags) and one case for which exposure to methamidophos was suspected but plausibly ruled out on investigation. Each exposure category is discussed in more detail below.

Comparison to other OP compounds - selection of case and control subjects

Of the 4,042 exposures with sufficient information to classify, 1,716 (42.5%) involved agricultural employment. The exposures related to agricultural employment including 401 subjects with ChE-related illness; five of these subjects were excluded because the OP compound involved was unknown or not specified in the investigation. The *case group therefore included 396 subjects*. Of the 1,315 subjects without demonstrable ChE-related illness, *758 (57.6%) met the criteria for inclusion as controls*. This group included 550 subjects with non-specific symptoms possibly compatible with ChE illness, but ChE values in the population normal range; 30 subjects who had symptoms compatible with ChE-related illness, but no change from baseline ChE activities (definite evidence of lack of ChE inhibition); 10 subjects who had unrelated medical diagnoses; 47 subjects who had one or more irritant symptoms and no symptoms compatible with ChE-related illness and no evidence of ChE depression; and 121 asymptomatic exposures who had no evidence of ChE depression. The total number of subjects meeting the criteria for inclusion in the study was thus 1,154. Separately published data indicate that the cases and controls are broadly representative of the California agricultural workforce.[25] Data on illness characteristics for the two groups are shown in Appendix 1. In the complete case file, 222 subjects had exposure to methamidophos (and other ChE inhibitors in 201 subjects) and 932 subjects had exposures to one or OP compounds other than methamidophos.

Odds ratios for methamidophos derived from the case-control study are shown in Table 2 by exposure strata. Methamidophos associated cases showed a significantly decreased frequency of ChE-related illness compared to other OPs in the overall study file (OR=0.32, $p<10^{-5}$). This decrease was associated principally with the 201 exposures to mixtures of ChE-inhibitors containing methamidophos (OR=0.31, $p<10^{-5}$). The 21 subjects with exposure to only methamidophos did not differ significantly in frequency of ChE illness from subjects exposed to other single OP compounds (OR=0.61, p=0.439).

Application associated exposures

Thirty-two reports involved workers with application exposures to methamidophos, including seven with direct exposure, 23 with routine application exposure, and two with documented violations of proper application procedure. Two additional subjects (2055-88 and 90-88) reported direct exposures to methamidophos but the investigation files did not include sufficient information on the nature of the symptoms or illness to classify them as either related or unrelated to cholinesterase inhibition (Table 3).

The 24 subjects with application exposure to methamidophos who met case-control criteria (Table 1, block 2) had a greater likelihood of ChE-related illness than the remaining 198 subjects with methamidophos exposure (OR=38.0, $p<10^{-5}$). In the case-control analysis (Table 2, block 1), the 24 subjects with methamidophos application exposure had a greater likelihood of ChE-related illness than the 228 subjects with application exposure to other OP compounds (OR=3.09, p=0.035). This finding did not achieve statistical significance when subjects with application exposure to single OP compounds and OP/carbamate mixtures were evaluated separately (Table 2, blocks 2 and 3).

Drift exposures

Drift exposures are cases of illness that occur as a result of dispersion of the material to an off-target site during application. Nine cluster episodes (Table 4) accounted for 203 (91.4%) of 222 drift exposure case to methamidophos. Five episodes (642-83, 933-83, 2903-87, 2179-85, 1954-89) each involving fewer than 10 individuals together, accounted for 16 cases. The remaining four episodes (306-88, 1297-83, 1644-83, 2175-82) involving from 11 to 131 individuals accounted for 187 cases, and the twenty remaining cases involved isolated exposures to individuals (Table 5).

The 181 subjects with drift exposure to methamidophos who met case-control criteria (Table 1, block 2) had an overall significantly reduced risk of ChE-related illness compared to 41 subjects with other types of methamidophos exposure (OR=0.05, $p<10^{-5}$). The drift exposures associated with methamidophos had a non-significantly reduced risk compared to the 287 exposures in the case-control study file (Table 2, block 1) associated with drift of other OP compounds (OR=0.51, p=0.058).

Field Residue Cases

Of the 55 field residue cases, 47 (85.5%) were associated with two cluster episodes resulting from early reentry into methamidophos treated fields (Table 8). The first episode (index case 980-86) involved a weeding crew of 25 workers who entered a cotton field treated earlier in the morning with methamidophos. The index case had symptoms of nausea, headache, dizziness, and salivation and one case reported only symptoms of burning of the lips and tongues. The remaining 23 cases reported compatible, but non-specific symptoms including headache, nausea, dizziness, vomiting, abdominal pain, nervousness, and diarrhea. Cholinesterase results were reported in the normal range for one worker, but were unavailable for the remainder of the crew.

The second large cluster episode involved 18 workers who briefly entered a cotton field treated with methamidophos in an effort to escape border patrol agents. Six of the workers had non-specific symptoms compatible with cholinesterase inhibition (principally headache), one report a rash on the upper arms, and eleven had no symptoms. Cholinesterase tests were drawn on 17 of the workers, but were not reported in the PISP file.

One case involving normal field reentry following methamidophos application to a tomato field (2368-85) resulted in definite cholinesterase poisoning. The worker was a member of a crew of twenty, but was apparently the only one to seek medical treatment and neither he nor the other workers were interviewed to determine the prevalence of symptoms in the remaining crew members. The worker with the reported illness showed a plasma cholinesterase below the lower limit of the population normal range on the day of his initial medical evaluation and a RBC cholinesterase within the population normal range. Six days later a followup sample showed a 12% increase in plasma and a 14% increase in RBC cholinesterase, but no further followup samples were available.

The only fatal case associated with exposure to methamidophos occurred in San Diego county where a field worker entered a tomato field treated with the material on the same day (see case 1837-85, Table 7). He felt faint in the field and collapsed. Other workers who were not reported to be ill, transported him to a hospital in Mexico where he was declared dead on arrival (DOA). Autopsy done at that hospital did not include evaluation of ChE levels and exact relationship between his death and the methamidophos exposure could therefore not be determined.

The 13 subjects with field residue exposure to methamidophos who met case control criteria (Table 1, block 2) did not differ significantly from other methamidophos exposed subjects in frequency of ChE illness (OR=0.90, p=1.000). Compared to 253 subjects with field residue exposures to other OPs (Table 2, block 1), the methamidophos exposed subjects, showed a reduced risk of ChE illness that was of borderline statistical significance (OR=0.21, p=0.061).

Discussion

Although the California PISP program offers a unique population based data source for evaluating the occurrence of pesticide illnesses, several limitations of the PISP data deserve consideration. For cases that are reported to the system, complete understanding of the exposure-illness relationship is hindered for some cases by lack of routine access to medical records to obtain test results where the cholinesterase test was ordered, and by the apparent failure of physicians to order cholinesterase analysis for others. Reporting of symptoms in medical records, PIRs, and DFRs may also be incomplete, so that the presence or absence of critical diagnostic signs may have been incompletely recorded on the available records. Understanding of the circumstances of exposure also may have been limited in some instances because of fear that disclosure of violations of regulatory requirements would result in enforcement penalties.

The limitations of the illness investigation process are critical to appreciate in evaluating the significantly increased frequency of ChE-related illnesses associated with the application of methamidophos (Table 2). Eleven (57.9%) of the 19 ChE-related application illnesses followed routine applications of methamidophos, implying that current practices for handling methamidophos deserve careful scrutiny. It was apparent, however, that no instances of ChE-related illness occurred among the small number of exposures reported following routine application of methamidophos as the sole ChE inhibitor.

Another important limitation of this study involves the unknown efficiency of case reporting.[26 27] This is particularly problematic in interpreting the lack of reports of OPIDN following serious cases (e.g. case 1352-83) of poisoning with methamidophos. This may have resulted from failure to reach the threshold of inhibition of neurotoxic esterase associated with OPIDN[28] that was apparently reached in some near fatal poisonings with methamidophos. In the absence of known clinical efforts to evaluate the possibility of OPIDN, this cannot be stated with certainty.

For exposure to methamidophos drift the risk of ChE-related illness showed a reduction compared to the risk for drift exposure to other OPs reported to PISP that was of borderline statistical significance (OR=0.51, p=0.058) . The overall frequency of ChE-related illness for all drift exposure cases was slight greater than 10% (Table 2). For field residue exposure, the risk of ChE illness also showed a non-significant reduction compared to other OPs (OR=0.21, p=0.061). These non-significant reductions in the frequency may simply derive from the element of chance involved in reporting of illness clusters in both the drift and field residue exposure categories. An alternative explanation is the heavy use of methamidophos on cotton, a crop involving minimal use of hand labor. One large cluster associated with field residue exposure illustrates the role of chance events in the occurrence of cluster episodes: workers fleeing the immigration service briefly entered a cotton field earlier treated with methamidophos. A second large cluster, also involving residue on cotton, was difficult to evaluate: workers had more prolonged opportunity for contact with methamidophos, but the investigation file contained cholinesterase data for only one worker.

Conclusion

The overall risk of ChE-related illness associated with exposure to methamidophos showed an overall reduction from that associated with other OPs reported to the California PISP system. This reduction in overall risk was attributable to the large percentage of methamidophos cases with relatively low risk drift exposures. For application associated methamidophos exposure, the risk of ChE-related illness appeared significantly increased compared to other OP compounds in the case-control study file.

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Table 1 Exposure versus Illness Category 1982-1990 Methamidophos Associated Cases n=315

Exposure Category	Illness Category						
	1=*Definite*	**2**=*Probable*	**3**=***Possible***	**4**=*Unlikely/ unrelated*	**5**=*Non-ChE effect*	**7**=*No symptoms*	**Row Total**
1=*Direct eye/skin exposure*	3	3	1				**7**
2=*Drift exposure*	13	1	135		13	60	**222**
2.1=*In field at time of application*			1				**1**
5=*Normal fieldwork*	1		3			1	**5**
5.1=*Irrigator early field reentry*			1				**1**
5.2=*limited contact early reentry*	1		6		1	11	**19**
6=*Violation of field reentry*		1	28		1		**30**
7=*Normal application*	11		8	3		1	**23**
8=*Violation of proper application procedure*	2						**2**
9.0=*Ingestion of pesticide residue*	1						**1**
10=*Other*	2		1				**3**
11=*No evidence of exposure*				1			**1**
Total	**34**	**5**	**184**	**4**	**15**	**73**	**315**
Methamidophos exposures that meet case-control selection criteria n=222							
1= *Direct eye/skin exposure*	3	3					**6**
2=*Drift exposure*	12	1	105		9	53	**180**
2.1=*In field at time of application*			1				**1**
5=*Normal fieldwork*	1					1	**2**
5.1=*Irrigator early field reentry*							**0**
5.2=*limited contact early reentry*					1	8	**9**
6=*Violation of field reentry*		1	1				**2**
7=*Normal application*	11		2	3			**16**
8=*Violation of proper application procedure*	2						**2**
9.0=*Ingestion of pesticide residue*	1						**1**
10=*other*	2		1				**3**
Total	**32**	**5**	**110**	**3**	**10**	62	222

Table 2 Methamidophos vs. OP exposures that did not involve methamidophos OP case control file n = 1,154

Case Control Status	Definite/ Probable Cases	Other	Total	Definite/ probable cases	Other	Total	Odds Ratio	p value
Exposure Category	*Methamidophos n=222*			*1982-1990 other OP cases n=932*			*Statistical Comparison*	
All application associated categories	19	5	24	183	149	332	3.09	0.037
Direct	6	0	6	68	25	93	Undefined	0.33
Normal application work	11	5	16	86	110	196	2.81	0.10
Violation of proper application procedure	2	0	2	29	14	43	Undefined	0.85
Drift	13	168	181	38	249	287	0.51	0.058
Overall Field Residue	2	11	13	116	137	253	0.21	0.061
Normal field reentry	1	10	11	81	98	179	0.12	.025f
Field reentry violation	1	1	2	35	39	74	1.11	1.00f
Overall File	37	185	222	359	573	932	0.32	<10-5

Subtotals shown in italics for application categories (direct exposure, normal application, and violation of proper application procedure) and field residue (normal field reentry and reentry violation). Total for overall file includes 65 miscellaneous exposures (4 methamidophos and 61 for other OPs) for which odds ratios were not calculated.

Methamidophos vs. other primary pesticide cases

Exposure Category	*Methamidophos as primary pesticide n=21*			*Other single OP pesticide cases n=586*			*Statistical Comparison*	
All application associated exposures	3	0	3	106	122	228	undefined	0.103f
Direct	3	0	3	46	22	68	undefined	0.547f
Drift	0	4	4	30	120	150	undefined	1.000f
All field Residue exposures	2	11	13	76	82	158	0.22	0.046
Normal field reentry	1	10	11	76	69	145	0.09	.014
Violation of field reentry	1	1	2	0	13	13	undefined	0.133
Overall	6	15	21	231	355	586	0.61	0.439

Subtotals shown in italics for application categories (direct exposure, normal application, and violation of proper application procedure) and field residue (normal field reentry and reentry violation). Total for overall file includes 51 miscellaneous exposures (one involving methamidophos and 50 involving other OPs) for which odds ratios were not calculated.

Table 2 Methamidophos vs. OP exposures that did not involve methamidophos OP case control file n = 1,154

Case Control Status	Definite/ Probable Cases	Other	Total	Definite/ probable cases	Other	Total	Odds Ratio	p value
Mixtures involving methamidophos versus mixtures of other OPs								
Exposure Category	*Methamidophos mixtures n=201*			*Mixtures of other OPs n=346*			*Statistical Comparison*	
All application associated categories	16	5	21	77	27	104	1.12	1.000f
Direct exposure	3	0	3	22	3	25	undefined	1.000f
Normal application work	11	5	16	39	24	63	1.35	0.83
Violation of proper application procedure	2	0	2	16	0	16	undefined	undefined
Drift	13	164	177	8	128	136	1.27	0.776
Overall file	31	170	201	128	218	346	0.31	<10-5

Subtotals shown in italics for application categories (direct exposure, normal application, and violation of proper application procedure) and field residue (normal field reentry and reentry violation). Overall file includes 14 miscellaneous exposures (3 for methamidophos and 11 for other OPs) for which odds ratios were not calculated. There were also 95 field residue exposures involving other OP compounds. Odds ratios not calculated because of lack of corresponding methamidophos cases.

Table 3 Application exposures

ID	Pesticides	Expo-class	CHE-norm	RBC-delta	Pla-delta	Ill-class	Hosp	Disab	Comment
2044-82	Methamidophos Copper hydroxide Chlorothalonil	1.0	3.0	U	U	1.0	0	0	Applying mixture of insecticide and fungicide to tomatoes; developed headache, diarrhea, increased secretion
2173-82	Methamidophos Methomyl Chlorothalonil	1.0	3.0	U	U	2.0	0	2	Uncoupled hose on closed system without releasing pressure and was sprayed with tank mix; developed weakness, headache, nausea, eyes twitching, blurred vision
1352-83	Methamidophos	1.0	4.1	72.22	94.18	1.0	2	U	Worker did not follow safety instructions and developed cramps, nausea, vomiting, and diarrhea.
1997-83	Methamidophos Chlorpyrifos	1.0	4.2	36.95	79.36	1.0	0	U	During work, spilled insecticide mixture on himself. Washed off, but felt ill afterwards and had depressed cholinesterase.
868-87	Methamidophos Methomyl	1.0	3.0	U	U	1.0	0	1	Applicator was sprayed with dilute pesticide when a hose broke. He developed nausea, stomach pains, bradycardia, muscle weakness, dizziness, diarrhea.
90-88	Methamidophos Methomyl	1.0	3.0	U	U	6.0	0	1	While spraying insecticide mixture on tomatoes, the hose broke and wet him with the material. He showered but later became ill despite wearing full safety gear. Nature of symptoms not specified in investigation
2043-88	Methamidophos	1.0	3.0	U	U	1.0	3	10	Mixer/loader splashed material on hand and body. Changed and washed but developed following symptoms: headache, stomach cramps, weakness, nausea, vomiting, blurry vision, bradycardia and shakes. ChE test-no results. Wearing coveralls, rubber boots and gloves, respirator eye protection.
2055-88	Methamidophos	1.0	3.0	U	U	6.0	0	0	Material splashed into face when opening container. Not wearing goggles or safety glasses. Container had built up some pressure before it was opened. No specific symptoms mentioned in investigation.
1957-84	Methamidophos Mevinphos Oxydemeton-methyl Demeton	1.0	4.1	38.68	70.49	1.0	2	U	While mixing insecticides, he splashed some on face and became ill. Symptoms included nausea, cramps and dizziness.

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Table 3 Application exposures

ID	Pesticides	Expo-class	CHE-norm	RBC-delta	Pla-delta	Ill-class	Hosp	Disab	Comment
Routine Application Associated Cases									
1596-83	Methamidophos	7.0	3.0	U	U	3.0	1	3.0	After mix/loading methamidophos, worker developed vomiting, stomach cramps, dizziness, and nausea.
2618-83	Methamidophos	7.0	5.0	U	U	3.0	0	3.0	Worker handled methamidophos and had history of cholecystitis. Symptoms included vomiting, weakness, nausea, lightheadedness.
605-84	Methamidophos Chlorpyrifos Disulfoton	7.0	1.0	0.00	0.00	3.0	30	3.0	A ground applicator became ill after pesticide applications between 4/12 and 5/9/84 when he had symptoms of nausea, vomiting, abdominal cramps, double vision, dry skin, weakness.
143-85	Methamidophos	7.0	3.0	U	U	3.0	2	3.0	Exposed to methamidophos while spraying cabbage field and developed nausea, headache, and vomiting.
1272-86	Demeton Diazinon Methamidophos	7.0	4.1	29.00	82.00	1.0	0	1.0	Applicator could not sleep and had sweaty palms, restlessness, tingling fingers. Applicator couldn"t identify a particular exposure incident, used protective equipment and closed system.
1539-86	Carbaryl Fenvalerate Methamidophos Methomyl	7.0	4.4	56.20	78.10	1.0	16	1.0	Wore all required clothing and equipment, also using closed system. Symptoms included nausea, vomiting, and dehydration.
231-87	Demeton Dimethoate Methamidophos Methomyl	7.0	4.0	0.00	0.00	3.0	0	3.0	Applicator felt weak and light headed. He had ChE blood test in the normal range and stated he had been working long hours and had consequently felt very tired recently.
955-88	Methamidophos	7.0	5.0	U	U	3.0	0	3.0	The driver of a nurse rig containing methamidophos experienced nausea and fainted while at work. He stated that the odor of the pesticide made him feel ill.
1300-88	Chlorpyrifos Dimethoate Methomyl Methamidophos	7.0	1.0	0.00	0.00	3.0	5	3.0	Developed tightness of chest, nausea and vomiting after mixing, loading pesticides. Worker used a closed system for category 1 materials. Wore respirator, protective clothing, and goggles.

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Table 3 Application exposures

ID	Pesticides	Expo-class	CHE-norm	RBC-delta	Pla-delta	Ill-class	Hosp	Disab	Comment
1673-88	Chlorpyrifos Dimethoate Methomyl Methamidophos	7.0	2.0	U	U	1.0	0	1.0	Six hours after leaving work, felt weak & nauseated. Diagnosis was acute & chronic pesticide poisoning.
2331-88	Methamidophos Profenofos	7.0	4.1	55.27	97.40	3.0	20	1.0	Loading pesticide, became ill felt nausea, blurred vision, weak and shaky. Supervisor states respirator, rubber gloves, coveralls, rubber boots and face shield worn.
2669-88	Chlorpyrifos Methamidophos Paraquat Pendimethalin	7.0	4.2	18.95	5.45	3.0	5	4.0	Had been mixing and loading, but was crushing pesticide container when he felt ill. Later in evening experienced loss of voice and developed stupor/comatose state. Reported to have used appropriate safety equipment.
1465-86	Methamidophos Methomyl Parathion Profenofos	7.0	4.1	97.46	73.06	1.0	29	1.0	Wore all safety equipment when mixing/loading. Symptoms included weakness, vomiting, headaches.
946-89	Oxydemeton methyl Mevinphos Methamidophos Acephate	7.0	4.2	68.16	67.44	1.0	U	1.0	Worker was mixing and cleaning application-related equipment when he developed headache, nausea, vomiting, muscle weakness, sweating, dizziness and constricted pupils.
908-88	Methamidophos Mevinphos	7.0	4.2	75.70	71.90	1.0	71	1.0	After mixing/loading various pesticides with a closed system he developed nausea, dizziness, and vomiting that became severe enough to require hospitalization.
1489-88	Methamidophos Methomyl Mevinphos	7.0	4.2	66.40	87.50	1.0	15	1.0	Worker was loading pesticides when he experienced weakness, nausea, vomiting, blurred vision despite use of respirator, face shield, rubber gloves and boots, coveralls.
2045-88	Methamidophos Methomyl Mevinphos	7.0	4.2	77.69	97.49	1.0	42	1.0	Mixer/loader developed weakness, blurred vision, nausea, vomiting, tiredness, excess salivation & dizziness. CHE: plasma - 2% of baseline; RBC - 22% of baseline. Wore coveralls, respirator, rubber gloves & boots and goggles.
860-85	Oxydemeton methyl Methomyl Methamidophos Mevinphos	7.0	4.2	67.86	74.65	1.0	U	1.0	Mixer/loader wore protective equipment but removed respirator at times for comfort. Symptoms included twitching eyes, numbness in hands, difficulty in breathing.

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Table 3 Application exposures

ID	Pesticides	Expo-class	CHE-norm	RBC-delta	Pla-delta	Ill-class	Hosp	Disab	Comment
2221-85	Demeton Methamidophos Mevinphos	7.0	1.1	0.00	0.00	4.0	0	4.0	Worker became ill (nausea, nervousness, elevated heart rate, irritated eyes.) after applying 3 cat I pesticides while wearing "all safety gear" including a respirator. Cholinesterase levels were higher than baseline levels on the day of the incident.
2060-84	Methamidophos Mevinphos Methomyl Acephate	7.0	4.1	49.68	44.63	7.0	20	7.0	Had no symptoms when routine blood test showed depressed CHE. He had been working with multiple CHE inhibitors during the previous week.
2270-90	Oxydemeton methyl Mevinphos Methamidophos Chlorpyrifos Acephate	7.0	4.2	0.00	10.05	4.0	0	4.0	Worker experienced nausea and dizziness after coming to work and making one application. Wearing resistant coveralls, gloves, boots, face shield, hat, respirator. CHE results within normal on that day, however one month later levels 35% below normal.
Violations of proper application procedures									
1397-86	Methamidophos Methomyl Mevinphos	8.0	4.1	67.00	23.00	3.0	U	1.0	Did not wear respirator while mixing/loading without closed system; developed nausea, vomiting, salivation, lacrimation, urination, gastrointestinal cramping, fasciculations and sweats.
1446-86	Methamidophos Mevinphos Oxydemeton methyl	8.0	4.4	21.00	0.00	1.0	49	1.0	Applicator was tired and sleepy at time routine ChE sample was found to be depressed. He apparently had not changed filter cartridges on his respirator for about 2 months.

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Table 4 Drift Cluster episodes

ID	Pesticides	Comment
306-88	Methamidophos Maneb	11 school instructors complained of a strong odor from an adjacent broccoli field being sprayed. Swab sample taken from light post between field & school was misplaced. Symptoms by teachers included sore eyes, nausea & tightness in throat. No cholinesterase tests reported on any of the teachers.
642-83	Demeton Methamidophos Sulfur	Employee and supervisor were reportedly drifted on from an application 1/4 mile away. Supervisor claims symptoms are odor-related, but employee did not notice a foul odor. Both had normal cholinesterase levels.
933-83	Methamidophos Oxydemeton-methyl Mevinphos	One employee developed nausea and headache and second developed nausea, facial numbness, and vomiting working downwind of field treated previous evening. Symptoms reportedly occurred as they moved toward the treated field. Neither had ChE levels included in investigation report.
1297-83	Methamidophos Oxydemeton-methyl	131 harvesters 1/8 mile from aerial application developed symptoms and emotional distress after smelling foul odor and observing helicopter. All sent to hospital after working 15 min. in the field. 76 developed compatible, but non-specific symptoms, including 73 who had normal ChE levels and 3 who had no ChE test reported. Four showed RBC ChE slightly below the normal laboratory range. Six had only irritant symptoms and 45 were asymptomatic.
1644-83	Methamidophos Oxydemeton-methyl Mevinphos	Twenty-five harvesters working 3/4 mile from aerial application, 11 developed compatible, but non-specific symptoms of OP poisoning, one had relatively specific symptoms suggestive of OP poisoning, thirteen remaining cases had only irritant symptoms or were asymptomatic including the only two workers with definite ChE depression.
2175-82	Methamidophos Oxydemeton-methyl Mevinphos Dithiocarbamate	Thinning crew was drifted on by aerial application one eighth of a mile away.
2179-85	Copper hydroxide Metalaxyl Methamidophos	School bus with 32 children and 1 adult (driver) was sprayed by a plane applying several pesticides. Two children complained of symptoms that included nausea, fainting and abdominal pain and one had a slightly depressed plasma ChE level. One asymptomatic child had a depressed RBC ChE level and two had levels in the normal range. Driver complained of irritated mouth but did not have ChE levels tested.
1954-89	Dimethoate Methamidophos Adjuvant	Three workers were cleaning seed when adjacent field (50') was sprayed. They smelled an odor but no noticeable drift. Developed headaches, dizziness and chest pain. One worker had decreased cholinesterase levels from normal range. Diagnosis - possible chemical exposure.
2903-87	Maneb Metalaxyl Methamidophos	While picking celery 3 workers became ill after smelling the odor from an application in an adjacent field following a shift in the wind. Symptoms included vomiting, dizziness, and irritated throats.

Table 5 Miscellaneous Drift Cases

ID	Pesticides	Expo-class	CHE norm	RBC-delta	PLA-delta	Ill-class	Hosp	Disab	Comment
1511-82	Methamidophos Demeton-methyl Chlorothalonil	2.0	3.0	U	U	3.0	0	0	Headache and nose bleed from possible drift complaint
837-83	Methamidophos	2.0	5.0	U	U	3.0	0	2	Contacted drift while riding in tractor; developed nausea and vomiting. Atropine administered.
996-83	Methamidophos	2.0	3.0	U	U	3.0	0	12	Was exposed to spray drift from neighboring field. developed headache, vomiting
1224-83	Methamidophos Oxydemeton-methyl Pyrethrins/piperonyl butoxide	2.0	4.0	0.00	0.00	3.0	0	0	Employee was weeding in field next to one being treated. Foreman stated he smelled a foul odor, though employee did"t mention this. Developed headache, nausea, blurry vision, lightheadedness.
896-83	Oxydemeton-methyl Methamidophos Pyrethrins/piperonyl butoxide	2.0	4.0	0.00	0.00	3.0	0	4	Employee fainted, and developed, weakness, dizziness, nausea, headache, intolerance to light while weeding broccoli. Field 1/4 mile away was being treated. Treatment history for broccoli field was 2 weeks previous (chlorpyrifos).
1225-83	Methamidophos Oxydemeton-methyl Permethrin	2.0	4.0	0.00	0.00	3.0	0	2	Employee was tying vines downwind from an application. Noticed a foul odor and developed headache, stomach disorder. Others in the crew noticed the odor, but did not report symptoms.
1526-84	Methamidophos	2.1	4.0	0.00	0.00	3.0	0	16	Irrigator accidentally sprayed by crop duster developed headache, nausea, and vomiting.
2495-84	Methamidophos	2.0	3.0	U	U	3.0	0	0	Resident of a mobile home park stated that, following a methamidophos application to a field across the road from his mobile home park, he developed a headache, vomiting, diarrhea, cramps, ear drainage, and a foul taste on his lips.
759-84	Methamidophos	2.0	1.0	0.00	0.00	3.0	0	2	Exposed to spray drift while working in field adjacent to pesticide application and developed chest pains, nausea, vomiting.
1648-86	Methamidophos	2.0	5.0	U	U	3.0	0	U	11 bank employees complained of odor following drift of methamidophos application made to adjacent field. 7 Employees developed symptoms including headaches, difficulty breathing, sore throat & eyes and 2 sought medical attention. Methamidophos residue found in air filters in vent.
1831-88	Chlorpyrifos Methamidophos	2.0	3.0	U	U	3.0	0	0	Resident developed headache & dizziness from an aerial application of a nearby cotton field. Field was about 1/4 mile from her home.

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ID	Pesticides	Expo-class	CHE norm	RBC-delta	PLA-delta	Ill-class	Hosp	Disab	Comment
2049-88	Methamidophos Profenofos	2.0	4.0	0.00	0.00	3.0	0	5	Worker became sick to stomach and developed headache from application to adjacent field. Blood tests in normal range. Worker felt odor was the problem; was not exposed to mist.
1749-88	Methamidophos Chlorothalonil Metalaxyl	2.0	5.0	U	U	3.0	0	0	Worker was hoeing weeds when he was drifted on by nearby application. Developed sore throat, burning eyes, nausea and diarrhea. Other workers in crew did not have symptoms.
1624-89	Methamidophos Copper hydroxide	2.0	1.0	0.00	0.00	3.0	0	4	Worker was cultivating in field adjacent to field sprayed earlier in day. Developed dizziness, headache, nausea. Could not smell "pesticide" odor. Diagnosed - exposure w/ secondary headache. CHE test "negative" (values not given).
1825-89	Chlorpyrifos Methamidophos	2.0	5.0	U	U	3.0	0	7	Mixer/loader was drifted on. Wearing rubber boots and gloves coveralls, respirator but no eye protection. Symptoms included headache, nausea, vomiting, fainting spell and burning eyes. He used a closed m/l system for his own work and drift was from an unrelated application.
1963-89	Methamidophos Dimethoate Copper Hydroxide Adjuvant	2.0	3.0	U	U	3.0	0	0	Worker was repairing irrigation pump when he noticed a chemical odor. He became nauseous, dizzy, vomited and had a headache. Site is commonly used for mixing/loading operations.
1141-86	Dimethoate Methamidophos Mevinphos	2.0	2.0	U	U	1.0	0	2	Applicator was exposed to spray mist while applying methamidophos, mevinphos & dimethoate. Was removed from applying insecticides until blood levels improved. He did not shower or change clothes after the application. Symptoms included pain in his eyes, vomiting, headache, aching in legs, stomach pains, diarrhea
2301-85	Demeton-methyl Methamidophos Mevinphos	2.0	4.0	0.00	0.00	3.0	0	U	Allegedly contacted spray drift from application in adjacent field and developed nausea, numbness, coldness in chest, dizziness
2883-90	Methamidophos	2.0	3.0	U	U	3.0	0	0	Air application to potato field. She experienced mist on her skin. Symptoms of nausea, vomiting occurred. Samples from her property and some hay samples confirmed drift occurred into the field she was in. Diagnosis-mild O.P. Poisoning.

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Table 6 Miscellaneous field residue exposure cases

ID	Pesticides	Expo-class	ChE-norm	RBC-delta	PLA-delta	Illclass	Hosp	Disab	Comment
1074-89	Azinphosmethyl Methamidophos Triadimefon Oxydemeton-methyl Disulfoton	5.2	4.2	20.18	28.00	1.0	0	3	Worker entered field before reentry interval was up. He complained of chills, fever, vomiting, diarrhea and feeling faint. Field sprayed with O.P's. Protective clothing used: cotton coveralls and gloves.
1476-83	Methamidophos Propargite	6.0	5.0	U	U	3.0	0	0	Worker violated reentry and developed vomiting, dizziness, headache
1538-89	Chloroxuron Prometryn Adjuvant Methamidophos	5.0	3.0	U	U	5.0	0	5	Irrigator picking up pipe in field developed rash over body and hands. Using normal work clothes, cotton gloves, and rubber boots. Had been taking acetaminophen with codeine. Rash over body and hands. Diagnosis-possible allergic reaction to spray or acetaminophen with codeine.
1630-89	Profenofos Methamidophos Propargite	5.0	5.0	U	U	3.0	0	0	Irrigator brushing against foliage while walking down rows and doing shovel work. Began experiencing chest tightness, dizziness, chills, nauseated feeling. Hat, rubber gloves, boot, long sleeve shirt, and pants worn. Possible organophosphate poisoning.
1732-90	Methamidophos Chlorpyrifos Adjuvant	5.0	5.0	U	U	3.0	0	0	While weeding developed rash on face, neck, hands and nausea, dizziness for 7 days. Diagnosed chemical exposure. Sought medical attention after work crew was laid off. Noticed odor in field.
1747-88	Methamidophos	5.0	5.0	U	U	7.0	0	0	Tractor driver was nervous about entering posted field that had been treated with methamidophos. Complained of feeling ill and was taken to the doctor. No symptoms listed.
1837-85	Fenvalerate Methamidophos	6.0	3.0	U	U	3.0	0	0	Worker felt faint and collapsed in a San Diego tomato field freshly sprayed with methamidophos. On arrival to hospital in Mexico subject was unable to be resuscitated. No ChE results available from autopsy.
1899-84	Methamidophos	6.0	5.0	U	U	3.0	0	0	Blurry vision, headache, eye irritation test plot
1929-83	Methamidophos Chlorpyrifos	5.0	5.0	U	U	3.0	0	5	Weeding in cotton field treated previous day and was wearing boots and rain gear, but he developed weakness, vomiting, nausea, and chest pains.

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Table 6 Miscellaneous field residue exposure cases

ID	Pesticides	Expo-class	ChE-norm	RBC-delta	PLA-delta	Illclass	Hosp	Disab	Comment
2041-90	Methamidophos Anilazine Sulfur Adjuvant	5.0	5.0	U	U	3.0	0	5	Hoeing tomatoes while wearing long sleeved shirt, pants, cap, rubber gloves. Smelled pesticide-like odor. Vomited in field and intermittently for the next two days. Also had symptoms of nausea, headache, of weakness. Source of odor was not determined. CHE test done, but no results given.
2117-89	Methamidophos Fenvalerate Mancozeb® Chlorothalonil	5.0	1.0	0.00	0.00	3.0	0	0	Headache, eye ache while cultivating the field adjacent to a field being treated. Worker noticed strong odor causing symptoms. As precautionary measure, he saw docotr. Lab results indicated ChE level within normal lab range.
2294-88	Copper Dimethoate Methamidophos Sulfur	5.0	4.0	0.00	0.00	3.0	0	1	Worker harvesting lettuce developed nausea, and dizziness. No others in field developed any symptoms. Field across rail road tracks was sprayed earlier in the day. She began working in field away from area near sprayed field.
2368-85	Methamidophos Metalaxyl	5.0	4.1	0.00	31.4	1.0	0	U	Worker developed headache and abdominal pain while working in a field previously sprayed (3 days) with category I and II pesticides. Worker may have harvested vegetables from fields which were posted.
2667-88	Methamidophos Oxydemeton-methyl	6.0	5.0	U	U	3.0	0	0	Contacted chemicals that were sprayed in field while setting up sprinkler pipe. Developed headache and nausea. No special safety equipment used. Worker entered in violation of reentry interval.

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Appendix 1

Comparison of case and control subjects by illness characteristics

The case and control subjects showed several minor, but statistically significant differences in demographic composition. The mean age for cases was 29.4 years of age and 31.6 for controls subjects. Males represented 87.6% of cases and only 76.5% of the control subjects. Hispanic surnames, by contrast, were more common among controls (86.7%) than among cases (73.5%). Control subjects were more likely than cases to work in crop production (69.4% of controls vs. 45.2% of cases) and cases were correspondingly more likely to work in agricultural services (54.3% of cases vs. 30.3% of controls). For individual SIC codes, cases were less likely than average to occur among vegetable and melon workers (0161), and more likely to occur among crop protection services workers (0721). Cluster episodes accounted for 173 (43.7%) of the 396 case subjects and for 514 (67.8%) of the 758 controls.

As indicated in the illness definitions, all of the cases had one or more symptoms compatible with ChE illness; however, compatible non-specific symptoms were all present in 575 (75.9%) of the control subjects. Of the 309 subjects with definite illness, 80 (25.9%) had one or more specific symptoms related to ChE depression. The probable cases by definition all had specific symptoms. Three (0.4%) of the control subjects had one or more specific symptoms, but showed no depression relative to baseline ChE measurements. Irritant symptoms were present in 114 (28.8%) of the cases and in 263 (34.7%) of the controls. Odor was noted to be present by 80 (20.2%) of the case subjects and by 370 (48.8%) of the controls.

Of the case group, 223 (56.3%) had reported ChE (either RBC or plasma) levels below the population range of normal (median RBC depression estimated from the midpoint of the normal range=47.6%, range 0-97.5%; median estimated plasma ChE depression was 59.1%, range 0-97.4%). Forty-two (10.6%) had both a baseline ChE test and followup at the time of illness (median depression from RBC baseline=48.8%, range 0-87.4%; median depression from plasma baseline=59.1%). Nine (2.3%) of the cases had followup tests (median RBC depression=22.0%, range 0-47.6%; median plasma depression=20.0%, range 0-89.3%). For 11 cases (2.9%) only plasma ChE was reported, with only the lower limit of the population range listed on the laboratory reports (median depression below the lower limit of normal=45.2%; range 0-81.2%). In the control group, 466 subjects (61.5%) had ChE levels in the population normal range (median RBC depression below midpoint of normal range=0.0%, range 0-47%; median plasma ChE depression=0.0%, range 0-75.0%). Nineteen (2.5%) of the control subjects had baseline tests (median RBC ChE depression=2.0%, range 0-19.0%; median plasma depression=1.3%, range=0-13.9%). Six (0.8%) of the control subjects had plasma ChE activity tested by a laboratory listing only the lower limit of normal on its reports; all had levels above the reference point.

The large differences in ChE activity between the case and control subjects were reflected in the information on hospitalization and disability. One hundred four (27.2%) of the case subjects spent one or more days in the hospital (median 2 days, range 1-48 days) compared to 16 (2.1% of the total) in the control group.

The individual compounds most frequently associated with exposure to both case and control subjects was mevinphos (158 cases [39.9%] and 337 controls [44.5%]). Other compounds accounting for 10 or more case subjects (with % of total case subjects and % of total control subjects as indicated) included methomyl (88 cases [22.2%] and 123 controls [16.2%]), oxydemeton-methyl (71 cases [17.93%] and 242 controls [31.9%]), parathion (55 cases [13.9%] and 93 controls [12.3%]), phosalone (51 cases [12.9%] and 11 controls [1.5%]), dimethoate (39 cases [9.8%] and 177 controls [23.4%]), methamidophos (37 cases [9.3%] and 186 controls [24.5%]), diazinon (35 cases [8.8%] and 31 controls [4.1%]), chlorpyrifos (24 cases [6.1%] and 52 controls [6.9%]), azinphos-methyl (14 case subjects [3.5%] and 34 controls [4.5%]), methidathion (12 cases [3.0%] and 28 controls [3.7%]), and demeton (10 cases [2.5%] and 5 controls [0.7%]).